Michigan Department of Community Health

MDCH

LabLink

Laboratory Information from the Michigan Department of Community Health - Bureau of Laboratories

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FROM THE DIRECTOR

Robert Martin, MPH, Dr.P.H.

In the introductory June 1995 issue of *LabLink*, I discussed our changing health care system and the need for clinical and public health laboratories to evaluate their roles in addressing the health of the community. Since that time, we have seen a continuing shift of health care delivery to health plans. Medicaid services will soon be delivered primarily through managed care organizations. These changes are important for clinical laboratories and they are important for public health laboratories.

In Fall 1996, the Michigan Public Health Institute, the Michigan Department of Community Health and the Michigan State University Institute for Managed Care initiated a dialogue with leaders from government, public health and clinical laboratories, professional organizations, manufacturing and academia. Our purpose was to begin to develop a better understanding of the national and state issues facing public and private medical laboratories. An eight-page publication describing presentations at that meeting is available upon request (*Changing Health Systems - Managed Care and Medical Laboratories*). At that symposium we addressed future challenges, the roles of public health and clinical laboratories, education and learning, and opportunities brought about during these times of change. We will be working with the Medical Services Administration to assure there is coordination and collaboration between health plans and public health agencies on communicable disease issues (screening, diagnosis and treatment) such as, but not limited to, HIV and other sexually transmitted diseases and laboratory diagnosis of tuberculosis. In addition, we will be addressing processes for cooperative efforts in outbreak investigation and appropriate specimen collection and transport related to disease outbreaks.

In the spring of 1997, the Michigan Department of Community Health, the Centers for Disease Control and Prevention and the Association of State and Territorial Public Health Laboratory Directors sponsored a two-part national teleconference in which forty-three states participated. The conference was entitled, *Partners for the Future: Exploring the Roles of Public Health Laboratories*. These teleconferences were described in a brief article in the last issue of *LabLink*.

The product of the two meetings is the development of a "white paper" that is in the process of completion. The purpose of the document will be to help address the next steps to be taken in developing a plan of action for the public health laboratories in partnership with clinical laboratories in Michigan. Specifically, we will be looking at issues such as electronic laboratory surveillance for diseases of public health importance, focused laboratory surveillance efforts for emerging infectious diseases (including emerging antimicrobic resistance), establishment of nosocomial infection control support activities, integration of regional public health laboratories in efforts related to food borne disease surveillance, and expansion of educational efforts to clinical laboratories and to local health departments.

The years ahead are likely to be challenging with change coming more rapidly than we might want. However, to the extent that we are open and are willing to recognize our respective roles in ensuring a healthy community, the task will be made easier. We look forward to working with many of you as we address these issues in the coming year.

As I stated in my first *LabLink* communication, we would like to use this information sheet as a forum for you as well. Please provide us with your comments and thoughts on these issues or any others relevant to the clinical and public health laboratory community.

HCV TESTING SOON TO BE AVAILABLE

Patty Clark, M.P.H., Viral Serology Unit

Hepatitis C Virus (formerly designated non-A, non-B hepatitis) has been implicated as the causative agent in a substantial portion of acute and chronic liver disease in the United States. Disease caused by HCV is clinically indistinguishable from hepatitis B, although chronicity rates differ dramatically. While only 2-10% of acute HBV infections develop into chronic disease, 70-80% of those with hepatitis C infections become chronically infected.[1] HCV infection has also been associated with cirrhosis of the liver and hepatocellular carcinoma.

HCV has a single-stranded positive-sense RNA genome. It has been classified as a distinct genus in the *Flaviviridae* family. There are 6 major genotypes. Genotypes 1, 2 and 3 have a broad distribution. Subtypes 1a and 1b are common in the United States. In vivo, the virus exists as a series of related, but immunologically distinct, variants termed quasispecies.[2] This virus has not yet been cultivated nor visualized by electron microscopy.

Antibody testing is available utilizing an ELISA procedure. Because the incubation period ranges from 5 to 10 weeks (although both shorter and longer periods have been noted)[1] these tests may have a prolonged window of seronegativity after acute infection. They also do not distinguish between acute, resolved and chronic infection. Currently, assays for the direct detection of HCV viral antigen are not available.

Anti-HCV testing is clinically important in the diagnosis of individuals with signs, symptoms, and biochemical evidence of hepatitis and patients with a history of NANBH. HCV has been identified as an Emerging Infectious Disease threat by the Centers for Disease Control and Prevention. Individuals at high risk for hepatitis C infection include transfusion recipients, IV drug users, dialysis patients, and health care workers.

The Michigan Department of Community Health will be accepting serum samples for hepatitis C antibody testing beginning approximately August 1, 1997. Submit 2 ml of serum in plastic vials labeled with the patient's name or unique identifier. The form required is the FB200 Virology Test Requisition. Use the "other" line on the bottom right hand side of the form in the Viral Serology box. Be certain the name on the submitted tube EXACTLY matches the name placed in the patient information boxes. Mismatched samples will not be tested. Request Unit #8 which contains a plastic submission tube, shipping materials and the FB200 form by phoning (517) 335-8059. Questions regarding specimen submission or testing should be directed to Patty Clark, Viral Serology Unit, at (517) 335-8102.

1. Rose, NR; Convay de Macario, E; Folds, JD; Lane, HC; Nakamura, RM; editors. 1997. *ASM Manual of Clinical Laboratory Immunology.* Fifth edition. American Society for Microbiology Press. Washington, D.C. pp. 702-718.

2. Nolte, FS. 1997. Laboratory Diagnosis of Hepatitis C. *Immunological Investigations.* 26(1&2):119-207.

Requests for Variant HIV Testing (HIV-1 subtyping and HIV-2 detection)

Garald A.Goza, M.S.
HIV/AIDS Surveillance Section

A group of HIV-1 viruses that cause AIDS but have extensive genetic divergence from the typical (group M) strains have recently been classified as group O viruses. These strains are not consistently detected by standard, licensed HIV serology. The first recognized case of HIV-1 Group O infection in the United States occurred in Los Angeles County, California in 1996. Another more familiar variant, HIV-2, is a related virus which also causes AIDS. Over 65 HIV-2 infections have currently been reported throughout the U.S.

To date, no divergent strains of HIV-1 have been detected in Michigan. However two cases of HIV-2 infection have been reported. One unusual, non-B subtype (subtype A/C) of Group M HIV-1 infection was also recently identified in Southeastern Michigan through synthetic peptide serotyping. (Group M subtype B is the common HIV-1 strain throughout the U.S. and Europe.)

Continued surveillance for HIV variants at the local level is important in monitoring potential emergent genotypes. Clinicians evaluating patients with suspect, atypical HIV infections are encouraged to contact the Michigan Department of Community Health (MDCH) for assistance with arranging further laboratory diagnostic tests.

☞ All initial requests for HIV-1 subtyping and HIV-2 detection should immediately be referred to the MDCH HIV/AIDS Surveillance Section office for consultation at 517-335-8165 (Lansing); or 313-876-0353 (Detroit).

☞ Laboratories in receipt of *previously drawn* specimens for HIV-2 testing **only** should promptly contact Debbie Stephens in the MDCH HIV Lab at 517-335-8098 to make arrangements to have the specimen transported.

HIV/AIDS Surveillance epidemiologists will coordinate submission of laboratory specimens to MDCH and/or CDC for supplemental testing and characterization of the HIV strain. Currently, both the MDCH and CDC labs offer HIV-2 testing, while HIV-1 subtyping is available only through the CDC. MDCH Surveillance staff will also collect other epidemiologic data such as patient clinical indices, risks for HIV exposure, travel history and prior history of blood donation.

Please note that the CDC laboratory cannot accept variant blood specimens from providers (either clinician offices or private laboratories) without prior notification and arrangements. This is because CDC requires patient names to be removed and pre-determined unique identifiers to be assigned, along with special procedures for specimen shipping. Hence, CDC routinely instructs callers to contact their individual state health department for instructions on how to proceed. Your cooperation in directing these inquiries to MDCH as above will facilitate this process.

COSTS OF STRAWBERRY ASSOCIATED HEPATITIS "A" OUTBREAK

William Hall, M.D.,
Communicable Disease Epidemiology Division

During March and April 1997, a large outbreak of hepatitis A was identified in several Calhoun and Saginaw County school systems. The outbreak was epidemiologically linked to the school lunch program and a frozen strawberry product. A total of 267 cases have been confirmed to date in Calhoun County and Saginaw County. The same contaminated product may have been served to school children in other Michigan counties. In addition to the effort expended by Calhoun and Saginaw Counties in the investigation and control of the outbreak, many other Michigan local health departments were called upon to organize mass immunization clinics to administer immune globulin (IG) prophylaxis to large numbers of exposed persons.

Michigan local health departments were recently surveyed by MDCH to determine: 1) the number of doses of IG administered to case contacts; 2) the number of doses of IG administered to people exposed to the possibly contaminated strawberries; 3) the number of person hours devoted to this activities; and 4) estimated expenses including wages, equipment, resources, mailing, and other expenditures related to this outbreak. Results the survey are now as follows:

1) 9450 doses of IG were administered to hepatitis A case contacts.
2) 8487 doses of IG administered to people exposed to the possibly contaminated strawberries.
3) 7324 person hours of work associated directly with the outbreak were done by local health department staff.
4) $314,134 were expended by local health departments on wages, benefits, indirect costs associated with the outbreak.

A total of 15,837 vials of IG were provided for distribution by the Michigan Biologic Products Institute. At $7.00 per vial, the market value of this IG was $110,895. MDCH costs are estimated at $18,974. Therefore, the total public sector costs are estimated to at $444,003.

Department of Community Health Director, James K. Haveman, Jr. has urged the Attorney General to aggressively pursue repayment of costs associated with the outbreak. "State and local agencies devoted time and resources to the investigation and control efforts relating to this outbreak. I feel strongly that those responsible must be held accountable for their actions and urge the Attorney General to vigorously pursue repayment." said Haveman.

The total cost of this outbreak to Michigan and its residents is well beyond the $444,003 public sector cost estimate. This estimate does not include the cost to Michigan residents associated with treatment of the 267 illnesses (count to 6/2/97) that occurred, nor any expense, inconvenience, or discomfort associated with receiving IG.

LABORATORY DIAGNOSIS OF LYME DISEASE

Barbara Robinson-Dunn, Ph.D.
Microbiology Section

The Second National Conference on Serologic Diagnosis of Lyme Disease sponsored by the American Society of State and Territorial Public Health Directors (ASTPHLD) was held in 1994. One recommendation from that meeting, was to require that results from a serological two-test method be used for reporting cases of Lyme disease. In 1996 an effort was made to determine the use and knowledge of this test in Michigan. A questionnaire on the two-test method was prepared and sent to 168 hospital and commercial laboratories in Michigan. A total of 144 laboratories replied for a final response rate of 85.7%.

Results obtained from the survey showed that very few Michigan laboratories (7.6%) perform Lyme disease testing. Five of the eleven laboratories that do perform the testing are either not aware of or are not using the serological two-test standard. Most of the laboratories that send specimens to a reference laboratory for Lyme disease testing are not aware of the testing standard nor the procedures utilized by the reference laboratory to analyze specimens for Lyme disease. Records are not maintained of the number of specimens sent to the reference laboratories for Lyme disease testing. Furthermore, when results of testing are received from the reference laboratories, they are not reviewed before being sent to the physicians submitting the specimens. Therefore, an accurate record of the number of tests performed and the number of positives recorded cannot be estimated for Michigan laboratories. It is evident that more needs to be done regarding implementation of the use of this standardized test method.

This is an important issue in a state such as Michigan with a very low endemic rate of Lyme disease. If you have questions about the type of testing being done for Lyme disease at the reference laboratory your facility uses, insist that they provide you with answers and that they perform the serological two-test methodology. As always, you can call MDCH at (517) 335-8067 with questions about testing for Lyme disease.

ARBOVIRUS TESTING AT MDCH

MDCH Laboratory has performed arbovirus testing during the summer months for several years. Testing is available from May through October each year using the IgM Capture ELISA procedure developed at the Centers for Disease Control. Specific analytes tested include St. Louis Encephalitis, California Encephalitis (LaCross strain) and Eastern Equine Encephalitis (EEE).

This summer we have not been able to procure a positive control serum for the EEE assay. Because of this, we will be forwarding all samples for EEE testing to CDC. We regret any inconvenience that may result from this increase in turn-around time. Next year we hope to be able to locate a positive control which will enable us to perform the assay in our laboratory. This change will not affect any other arboviral testing. SLE and CEV testing are still being performed in our virology laboratory. If you have any questions on test availability, please phone Patty Clark, Viral Serology Unit, at 517-335-8102.

Contact the *LabLink* by phone at (517) 335-9763
or by e-mail at shifletts@state.mi.us

MICROBIOLOGY NEWS

Barbara Robinson-Dunn, Ph.D.
Microbiology Section

NEISSERIA MENINGITIDIS MENINGITIS IN MICHIGAN

Neisseria meningitidis continues to be an important cause of bacteremia and meningitis in Michigan. Recently, the Microbiology Section analyzed isolates submitted over the last 18 months. The following 59 sterile-site isolates were identified.

Grp/Source	B	C	Y	W135
Blood	7	9	16	1
CSF	4	9	5	
Other		6	2	
Total	11	24	23	1

It appears that disease due to serogroup Y is increasing, while that due to serogroup B is decreasing. Reports from the Centers for Disease Control and Prevention indicated that the increase in serogroup Y is also being noted in other parts of the country. In the past, serogroup Y has been known for its association with pneumonia and other respiratory illnesses. It appears now to be responsible for a majority of the cases of meningococcal bacteremia.

During December 1996 and early 1997, mid-Michigan experienced a few cases of meningitis due to *N. meningitidis*. Despite the claimsof the news media, there was not an "outbreak" of meningococcal disease. Isolates of *N. meningitidis* which were of the same serogroup were subjected to molecular analysis and were shown to be of different genotypes. Despite these findings, there was a great deal of concern every time the news announced another case of meningitis (the differentiation between bacterial and viral meningitis was lost on the lay public!).

Unfortunately, many microbiology laboratories no longer serogroup isolates of *N. meningitidis*. Others will test isolates for serogroup B and the pooled serogroups A,C,Y and W135. If the pool is positive no further serogrouping is done. We would urge all laboratories to submit **sterile site** isolates of *N. meningitidis* to MDCH for complete serogrouping. Allowing MDCH to determine the serogroup of isolates of *N. meningitis* will help us analyze meningococcal activity statewide. Additionally, isolates will be placed into our culture collection so that if an outbreak occurs, the bacteria will be available for molecular analysis.

SAFETY IN THE TUBERCULOSIS LABORATORY

On April 28, 1997, the Federal Register published a document entitled, "Goals for Working Safely with *Mycobacterium tuberculosis* Complex Species in Clinical, Public Health, and Research Laboratories". The purpose of this document is to update the Agent Summary Statement for *M. tuberculosis* as published in the 3rd edition of the CDC/NIH publication, *Biosafety in Microbiological and Biomedical Laboratories* (BMBL). CDC is requesting comments concerning this update which, if left unchanged, will have far-reaching effects on those microbiology laboratories performing mycobacteriology.

Because until recently, there had been few changes in the techniques available to laboratorians working with *M. tuberculosis*, these recommendations have remained the same through the last three editions of the BMBL. Recent changes in public health recommendations for use of rapid laboratory diagnostic procedures and the development of new technologies led CDC and a group of consulting laboratorians to review existing safety guidelines for working with *M. tuberculosis*. Revisions were presented and discussed at the Second National Conference on Laboratory Aspects of Tuberculosis, convened by the Association for State and Territorial Public Health Laboratory Directors and CDC in 1995. This report updates and expands those sections of the BMBL that address engineering controls, administrative practices and specific procedures for laboratorians who manipulate clinical specimens and purified cultures of *M. tuberculosis*, *M. africanum* and *M. bovis*.

This document can be retrieved from the following web site:http://www.access.gpo.gov/su_docs/aces/aces140.html. You will need to indicate that it is a Notice, the date is 04/28/97 and Centers for Disease Control. The period for comments has been extended until July 27, 1997. Please let your "thoughts backed by scientific data" be known.

Dr. Kenneth R. Wilcox receives "Pump handle" Award

Dr. Kenneth Wilcox, a former State Laboratory Director, and current State Epidemiologist, received the prestigious "Pump Handle" Award from his colleagues at the annual Conference of State and Territorial Epidemiologists (CSTE) in June. A single award is given annually to a member of CSTE in recognition of a career of epidemiologic achievement and outstanding service in the field of public health. For those of you who may not recall the significance of the 'pump handle,' in the 1850's, John Snow, a British physician, is credited with halting the spread of a cholera epidemic in London, England by removing the pump handle from a contaminated well - an effective epidemiologic control measure.

The HRA Laboratory QA/QC Grant

Michael O'Keefe, HRA QA/QC Coordinator

The Great Lakes Human Health Effects Research Program (GLRP) of the Agency for Toxic Substances and Disease Registries (ATSDR), sponsors nine studies involving human cohorts from New York to Minnesota. Each of the studies involves assessment of exposure to pollutants with methods ranging from gas chromatography to mass spectrometry and atomic absorption spectroscopy. A Quality Assurance / Quality Control Program was developed by the Health Risk Assessment Laboratory (HRA Lab) under a grant from ATSDR. The program's mission was to develop reference materials, distribute them throughout the Great Lakes basin, and to collate the results in order to establish data comparability between the labs receiving GLRP grants. These nine studies examine nine matrices and nineteen analytes. Matrices include blood and/or serum, breast milk, hair, and other human specimens. Analytes in the studies include PCB congeners, DDE, other pesticides, mercury, lead, and dioxins.

Manufacturing, distribution, and documentation necessary for the program were considered when developing these materials. Considerations for the matrix were; compatibility with the studies, availability of large quantities, and low background. Factors for analyte selection were commonality among the studies, availability, and interference from other potential analytes. The levels of the analytes were to meet the capabilities of the labs involved and be well above background interference levels, but they would mimic levels found in real human samples. The HRA Lab elected to produce one blank and one spiked reference material in ovine serum from the MDCH herd. The analytes were DDE and nine PCB congeners with spike levels in the range for a "Typical Fisheater" (0.5 to 5 ppb for each congener).

The manufacture and distribution involved collection, processing, and pooling of ovine serum, dispensing, before and after addition of the analytes, then freezing and shipping the frozen blank and spiked Reference Materials (RM's). Documentation to accompany the RM's included information for proper storage, handling and analysis of the RM's, MSDSs for the blank and spike, reporting forms and protocols for methods as well as for results. Data from the reports documented analytical similarities and differences. Feedback was designed into the system to document problems and solutions.

Distribution and verification of the RM's began simultaneously. The HRA laboratory initiated a complex characterization involving multiple extraction techniques and multiple analytical methods. CDC, acting as the reference laboratory, also analyzed the RM's. The participant labs were instructed to characterize the RM's by their individual study methods (at least 20 replicates) for use in intralaboratory monitoring and interlaboratory monitoring. The confidentiality of the participants was maintained by issuing a three letter code for each lab.

Initial feedback after distribution of the RM's was mixed. Some of the complaints included, "concentrations are too high,"and "additional analytes are needed." Conclusions drawn from these responses were that the fisheater data does not represent all of the Great Lakes, and the reference material program needed modification. The QA/QC reference materials program evolved based on feedback about the RM's from the labs.

To respond to the needs of the participants, another project, the QA/QC performance testing (PT) program, was initiated. The PT program allows the flexibility of different analytes at different levels than the RM program. The matrix can be ovine whole blood or serum. The potential analytes include a larger group of PCB congeners, pesticides, and heavy metals, that can be spiked at various levels. The key to this program is development and distribution of small batches of less complex (two to eight) unknowns on a quarterly basis. This will allow the occasional matching of the matrix / analyte / concentration to an individual study and result in faster turn-around time.

Data from both the RM and PT projects will lead to the QA/QC program goal of establishing comparability between the data from all of the laboratories under ATSDR's Great Lakes Research Program. Comparability will allow method to method and cohort to cohort comparisons by permitting the establishment of a basin wide database. The database will then be used to identify gaps in existing data and point toward future research.

Antimicrobial Resistance Trends, Regions One (Reg1, Detroit Area) and Two to Twelve (Reg2-12,Outstate Michigan)
Penicillin Resistant Study-site[1] Isolates of *Streptococcus pneumoniae*
and Vancomycin Resistant Sterile-site[2] Isolates of *Enterococcus spp.*
Michigan Sentinel Hospital Laboratory Survey, Fourth Quarter, 1995 through First Quarter, 1997

Percent Resistant[3]

		1995 Quarters				1996 Quarters						1997 Quarters	
	Resistance	Fourth		First		Second		Third		Fourth		First	
Microorganism	Classification[3]	Rg 1	Rg 2-12	Rg 1	Rg 2-12	Rg 1	Rg 2-12	Rg 1	Rg 2-12	Rg 1	Rg 2-12	Rg 1	Rg 2-12
Str. pneumoniae	Moderate or High	20	14	20	19	23	20	34	20	26	14	28	16
Str. pneumoniae	High Level only	5	4	5	2	5	3	9	4	8	4	10	5
E. faecalis	Resistant	1	0	2	1	1	0	3	1	3	1	3	1
E. faecium	Resistant	33	7	37	13	48	9	35	5	44	9	42	6
Total *Enterococcus*	Resistant	7	1	9	3	10	2	9	3	10	2	15	2

[1] Study sites = blood, CSF, deep surgical wound, pleural fluid(fl.), peritoneal fl., respiratory specimens or synovial fl.

[2] Sterile sites = blood, CSF, deep surgical wound, pleural fluid(fl.), peritoneal fl., or synovial fl.

[3] NCCLS, Performance Standards for Antimicrobial Susceptibility Testing, M100-S7.

LabLink is published quarterly by the Michigan Department of Community Health, Bureau of Laboratories, to provide laboratory information to Michigan Health professionals and the public health community.

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